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wherein:

Q1

n is the number of different molecules in the sample; N_i is the number of i^{th} molecules in the sample; and

 M_i is the mass of the i^{th} molecule.

a²

- 7. (Amended) The mixture according to Claim 1, wherein the oligomer is covalently coupled to Lys^{B29} of the human insulin drug.
- oligomer has an increased resistance to degradation by chymotrypsin when compared to the resistance to degradation by chymotrypsin of a polydispersed mixture of insulin drug-oligomer conjugates having the same number average molecular weight as the mixture.
 - 16. (Amended) A mixture of conjugates, each comprising insulin coupled to an oligomer that comprises a polyethylene glycol moiety, wherein the mixture has a dispersity coefficient (DC) greater than 10,000, where

$$DC = \frac{\left(\sum_{i=1}^{n} N_{i} M_{i}\right)^{2}}{\sum_{i=1}^{n} N_{i} M_{i}^{2} \sum_{i=1}^{n} N_{i} - \left(\sum_{i=1}^{n} N_{i} M_{i}\right)^{2}}$$

04

wherein:

n is the number of different molecules in the sample;

N_i is the number of ith molecules in the sample; and

M_i is the mass of the ith molecule; and

wherein the conjugate comprises a first oligomer and a second oligomer; and wherein the first oligomer is covalently coupled at Lys^{B29} of the insulin and the second oligomer is covalently coupled at N-terminal A1 or N-terminal B1 of the insulin.

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- 17. (Amended) The mixture according to Claim 1, wherein the human insulin drug is covalently coupled to the oligomer.
- 18. (Amended) The mixture according to Claim 16, wherein the insulin is covalently coupled to at least one of the oligomers by a hydrolyzable bond.
- 19. (Amended) The mixture according to Claim 16, wherein the insulin is covalently coupled to the polyethylene glycol moiety of at least one of the oligomers.

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- 20. (Amended) The mixture according to Claim 16, wherein at least one of the oligomers comprises a lipophilic moiety covalently coupled to the polyethylene glycol moiety.
- 21. (Amended) The mixture according to Claim 16, wherein at least one of the oligomers comprises a lipophilic moiety.
- 22. (Amended) The mixture according to Claim 21, wherein the insulin is covalently coupled to the lipophilic moiety.
- 25. (Amended) The mixture according to Claim 16, wherein the first and the second oligomers are the same.

 α^{ς}

26. (Amended) The mixture according to Claim 16, wherein at least one of the oligomers comprises a first polyethylene glycol moiety covalently coupled to the insulin by a non-hydrolyzable bond and a second polyethylene glycol moiety covalently coupled to the first polyethylene glycol moiety by a hydrolyzable bond.

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- 27. (Amended) The mixture according to Claim 26, wherein the oligomer(s) comprising a first polyethylene glycol moiety covalently coupled to the insulin by a nonhydrolyzable bond and a second polyethylene glycol moiety covalently coupled to the first polyethylene glycol moiety by a hydrolyzable bond further comprise a lipophilic moiety covalently coupled to the second polyethylene glycol moiety.
- 28. (Amended) The mixture according to Claim 16, wherein each of the conjugates is amphiphilically balanced such that each conjugate is aqueously soluble and able to penetrate biological membranes.
- 30. (Amended) A method of treating insulin deficiency in a subject in need of such treatment, said method comprising: administering an effective amount of the composition of claim 1 to the subject to treat the insulin deficiency.
 - 46. (Amended) A mixture of conjugates, each comprising an insulin drug coupled to an oligomer that comprises a polyethylene glycol moiety, said mixture having a molecular weight distribution with a standard deviation of less than about 22 Daltons, wherein the insulin drug is human insulin, and the oligomer is covalently coupled to Lys^{B29} of the human insulin and has the formula:

50. (Amended) A mixture of conjugates, each comprising an insulin drug coupled to an oligomer that comprises a polyethylene glycol moiety,

wherein each polyethylene glycol moiety has the same number of polyethylene glycol subunits,

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wherein each oligomer is covalently coupled to Lys^{B29} of the human insulin and has the formula:

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wherein the mixture has a molecular weight distribution with a standard deviation of less than about 22 Daltons.

52. (Amended) A mixture of conjugates in which each conjugate is the same and has the formula:

wherein:

B is carbonyl;

L is a linker moiety;

G, G' and G" are individually selected spacer moieties;

R is C₅ alkylene and R' is polyethylene glycol having 7 polyethylene glycol subunits;

T is methoxy;

j is 0 or 1;

k, m and n are 0; and

p is an integer from 1 to the number of nucleophilic residues on the insulin drug.

Please add the following new claims:

- 68. (New) The mixture according to claim 16, wherein at least one of the oligomers comprises a polyethylene glycol moiety having at least 2 polyethylene glycol subunits.
- 69. (New) The mixture according to claim 16, wherein at least one of the oligomers comprises a polyethylene glycol moiety having at least 5 polyethylene glycol subunits.